

## SPECIALTY GUIDELINE MANAGEMENT

### NEULASTA (pegfilgrastim) FULPHILA (pegfilgrastim-jmdp) UDENYCA (pegfilgrastim-cbqv) ZIEXTENZO (pegfilgrastim-bmez)

#### POLICY

#### I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

##### A. FDA-Approved Indication

###### **Neulasta**

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy  
Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
2. Hematopoietic Syndrome of Acute Radiation Syndrome  
Neulasta is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

###### **Fulphila**

Patients with Cancer Receiving Myelosuppressive Chemotherapy  
Fulphila is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

###### **Udenyca**

Patients with Cancer Receiving Myelosuppressive Chemotherapy  
Udenyca is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

###### **Ziextenzo**

Patients with Cancer Receiving Myelosuppressive Chemotherapy  
Ziextenzo is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

*Limitations of Use: Ziextenzo is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.*

##### B. Compendial Use

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1. Stem cell transplantation-related indications
2. Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
3. Radiation therapy/injury
4. Hairy cell leukemia
5. Chronic Myeloid Leukemia (CML), treatment of resistant neutropenia due to tyrosine kinases inhibitor therapy

All other indications are considered experimental/investigational and are not a covered benefit.

## II. REQUIRED DOCUMENTATION

### A. Primary Prophylaxis of Febrile Neutropenia

1. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the patient's risk factors that confirm the member is at high risk for febrile neutropenia.

## III. CRITERIA FOR INITIAL APPROVAL

### A. Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy<sup>1-6</sup>

Authorization of 6 months may be granted for prevention of febrile neutropenia when all of the following criteria are met (1, 2, 3, and 4):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving concurrent chemotherapy and radiation therapy.
3. The requested medication will not be administered with weekly chemotherapy regimens.
4. One of the following criteria is met (i or ii):
  - i. The requested medication will be used for primary prophylaxis in members with a solid tumor or non-myeloid malignancies who have received, are currently receiving, or will be receiving myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (*See Appendix A*) OR 10 – 19% risk of FN (*See Appendix B*) and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
    - a. Active infections, open wounds, or recent surgery
    - b. Age greater than or equal to 65 years
    - c. Bone marrow involvement by tumor producing cytopenias
    - d. Previous chemotherapy or radiation therapy
    - e. Poor nutritional status
    - f. Poor performance status
    - g. Previous episodes of FN
    - h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
    - i. Persistent neutropenia
  - ii. The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and scheduled planned for the current cycle (for which primary prophylaxis was not received).

### B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Stem cell transplantation-related indications

2. Radiation therapy/injury
  - i. Manage neutropenia in members acutely exposed to myelosuppressive doses of radiation therapy
  - ii. Treatment of radiation injury
3. Hairy cell leukemia  
Individuals with hairy cell leukemia with neutropenic fever following chemotherapy.
4. Chronic Myeloid Leukemia  
Individuals with Chronic Myeloid Leukemia (CML) for treatment of resistant neutropenia due to tyrosine kinase inhibitor therapy

#### IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

#### V. APPENDIX

##### A. APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher

1. Acute Lymphoblastic Leukemia:  
Select ALL regimens as directed by treatment protocol (see NCCN guidelines)
2. Bladder Cancer:
  - i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
  - ii. CBDCA/Pac (carboplatin, paclitaxel)
3. Bone Cancer
  - i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
  - ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
  - iii. Cisplatin/doxorubicin
  - iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
  - v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
  - i. Docetaxel + trastuzumab
  - ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
  - iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
  - iv. AT (doxorubicin, docetaxel)
  - v. Doc (docetaxel)
  - vi. TC (docetaxel, cyclophosphamide)
  - vii. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:  
FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)
6. Esophageal and Gastric Cancers:  
Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma  
TPF (docetaxel, cisplatin, fluorouracil)
8. Hodgkin Lymphoma:
  - i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
  - ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:  
Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:

- i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
  - ii. ICE (ifosfamide, carboplatin, etoposide)
  - iii. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
  - iv. MINE (mesna, ifosfamide, novantrone, etoposide)
  - v. DHAP (dexamethasone, cisplatin, cytarabine)
  - vi. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
  - vii. HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
  - viii. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:  
Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
12. Multiple myeloma:
- i. DT-PACE (dexamethasone/ thalidomide/ cisplatin/ doxorubicin/ cyclophosphamide/ etoposide) + bortezomib (VTD-PACE)
  - ii. DT-PACE  
(dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)
13. Ovarian Cancer:
- i. Topotecan
  - ii. Docetaxel
14. Pancreatic Cancer:  
FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
- i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
  - ii. Doxorubicin
  - iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
- i. Top (topotecan)
  - ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular cancer:
- i. VeIP (vinblastine, ifosfamide, cisplatin)
  - ii. VIP (etoposide, ifosfamide, cisplatin)
  - iii. TIP (paclitaxel, ifosfamide, cisplatin)

**B. APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%**

- 1. Occult primary – adenocarcinoma:  
Gemcitabine/docetaxel
- 2. Breast cancer:
  - i. Docetaxel
  - ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
  - iii. CA (doxorubicin, cyclophosphamide) (60 mg/m<sup>2</sup>) (hospitalized)
  - iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
  - v. AC + sequential docetaxel + trastuzumab
  - vi. A (doxorubicin) (75 mg/m<sup>2</sup>)
  - vii. AC (doxorubicin, cyclophosphamide)
  - viii. CapDoc (capecitabine, docetaxel)
  - ix. Paclitaxel every 21 days

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3. Cervical Cancer:
  - i. Irinotecan
  - ii. Cisplatin/topotecan
  - iii. Paclitaxel/cisplatin
  - iv. Topotecan
4. Colorectal:
  - i. FL (fluorouracil, leucovorin)
  - ii. CPT-11 (irinotecan) (350 mg/m<sup>2</sup> q 3 wk)
  - iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
  - i. Irinotecan/cisplatin
  - ii. Epirubicin/cisplatin/fluorouracil
  - iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's lymphomas:
  - i. EPOCH-IT chemotherapy
  - ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
  - iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
  - iv. FMR (fludarabine, mitoxantrone, rituximab)
  - v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
  - vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
  - vii. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
  - viii. Bendamustine
7. Non-Small Cell Lung Cancer:
  - i. Cisplatin/paclitaxel
  - ii. Cisplatin/vinorelbine
  - iii. Cisplatin/docetaxel
  - iv. Cisplatin/etoposide
  - v. Carboplatin/paclitaxel
  - vi. Docetaxel
8. Ovarian cancer:
  - Carboplatin/docetaxel
9. Prostate cancer:
  - Cabazitaxel
10. Small Cell Lung Cancer:
  - Etoposide/carboplatin
11. Testicular Cancer:
  - i. BEP (bleomycin, etoposide, cisplatin)
  - ii. Etoposide/cisplatin
12. Uterine sarcoma:
  - Docetaxel

## VI. REFERENCES

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